DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/1/10 has been entered.

Response to Amendments

Applicant's amendments filed 3/1/10 to claims 1-5, 8, 10, 14-18, 21, 23, 27-45, 47, and 49 have been entered. No claims have been canceled in this reply. Claim 51 has been added. Claims 1-5, 7, 8, 10, 14-18, 20, 21, 23, and 27-51 remain pending in the current application, of which claims 1-5, 7, 8, 10, 14-18, 20, 21, 23, and 27-50 are being considered on their merits. Claim 51 is withdrawn from consideration at this time since it is drawn to a nonelected species, imidazolidinyl urea. References not included with this Office action can be found in a prior action. Any rejections of record not particularly addressed below are withdrawn in light of the claim amendments and applicant's comments.

Election/Restrictions

Applicant's elections of the species "diazolidinyl urea," "EDTA," "whole blood," and "a packaging means for transporting said collection device" in the reply filed on

3/29/06 and the species "a flow cytometer" and "HIV" in the reply filed on 2/18/09 are still in effect over the claims.

Claim Objections

Claim 43 is objected to because of the following informalities: It should recite "K_3EDTA." Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5, 7, 8, 10, and 28-33 are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter which applicants regard as their invention. Evidence that claims 1-5, 7, 8, 10, 14-18, 20, 21, 23, and 34-39 fail to correspond in scope with that which applicants regard as the invention can be found in the replies filed 7/20/09 and 3/1/10. In the 7/20/09 remarks, applicant has stated, "The amended claims clearly set forth the feature that the amount of the compound is very small relative to the final volume within the container or tube **once the sample is drawn.**" See reply, page 21, paragraph continuing from previous page; emphasis added. Applicant further urges that "the claims … do not recite cells as a necessary component of the device." See 7/20/09 reply, page 20, paragraph 2. In the 3/1/10 reply, applicant alleges that claim 1 does require the presence of cells. See page 1. This statement indicates that the invention is different from what is defined in the claim(s) because the ratio between the volume of the compounds within the tube and the volume of cells collected into the tube is repeatedly cited by applicant as the basis for

patentability in the invention. See, for example, the 3/1/10 reply at page 2. The examiner submits that the claims do not actually define the invention, given applicant's urging that the volume ratio is inventive.

Because claims 2-5, 7, 8, 10, and 28-33 depend variously from indefinite claims 1 and 14 and do not clarify these points of confusion, they must also be rejected under 35 U.S.C. 112, second paragraph.

In the 3/1/10 reply, applicants allege that the claims do require that cells be present, but the examiner disagrees. There is no step in claim 1 in which mammalian cells are collected, just numerous limitations that describe what happens if they are collected.

Claims 1-5, 7, 8, 10, 14-18, 20, 21, 23, 27-39, 43, 44, 49, and 50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is drawn to "a method for collecting mammalian cells" comprising providing "a tube … that receives cells collected directly from a blood draw," but the claims do not include any clear step in which cells are necessarily collected. The claims should be amended such that they include all essential active steps, especially in view of applicants' insistence that the volume ratio between cells and compounds is inventive.

Because claims 2-5, 7, 8, 10, and 30-33 depend from indefinite claim 1 and do not clarify the point of confusion, they must also be rejected under 35 U.S.C. 112, second paragraph.

Claim 14 is drawn to a device for collecting mammalian cells and requires that the container is such that the ratio of preloaded compounds to "any cells collected into the container" is a particular value. However, it is not clear if the "any cells" in element (b) are necessarily the mammalian cells of the preamble and only those cells. Other cells could be placed into the tube. Clarification is required. Claim 27 suffers similar deficiencies.

Furthermore, claim 14 requires that the container "can maintain [a particular] internal pressure," but it is not clear whether a container must actually maintain that pressure to be encompassed by the claims or whether it must simply have that ability under some conditions. Clarification is required.

Because claims 15-18, 20, 21, 23, 28, 29, 34-39, 49, and 50 depend variously from indefinite claims 14 and 27 and do not clarify the point of confusion, they must also be rejected under 35 U.S.C. 112, second paragraph.

Claim 3 requires that the concentration of fixative in the tube be "less than about 1g/mL of preloaded compounds," but it is not clear whether the "mL" refers to the volume of the tube or to the total volume of preloaded compounds (i.e., the fixative accounts for 1g of the total 1mL of the total preloaded compounds). Clarification is required. Claims 4, 16, 17, 30-33, 36-39, 43, and 44 suffer similar deficiencies.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 7, 8, 10, 14-17, 20, 21, 23, and 27-50 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Ryan (1998, U.S. Patent 5,849,517; reference A3 on 2/20/09 IDS) taken in view of Camiener (1999, U.S. Patent 5,977,153; reference A4 on 2/20/09 IDS) and Glover et al. (1975, U.S. Patent 3,879,295) and Louderback (1976, U.S. Patent 3,973,913). In the interest of compact prosecution, the claims are interpreted as being drawn to a collection device comprising an anticoagulant and diazolidinyl urea (DU, a fixative), wherein the device has at least a partial vacuum inside. Some claims are drawn to methods for making and using such a device. In some dependent claims, the anticoagulant is EDTA. In some dependent claims, the cells to be preserved are those in whole blood. In some dependent claims, the components in the device are sterilized and/or freeze-dried. Some claims list downstream applications for the device.

Ryan teaches collecting whole blood samples in a vacutainer containing EDTA and adding a fixative solution containing DU, then processing the sample using flow cytometry (Specific Examples I and II at columns 8-9). Ryan teaches that the amount of DU to include in the collection device is that effective to fix or stabilize cells and tissues

while preserving antigenic sites thereof (column 7, lines 39-45; see also column 6, lines 56-60, and column 3, lines 30-39). Ryan teaches that the amount of DU may vary (column 4, lines 49-51; column 17, line 66, through column 18, line 1; and claims 4, 8, and 19). Ryan teaches that whole blood preserved in their device may be screened for HIV (Specific Examples XIII and XIV at columns 16-18). Ryan teaches that DU is a disinfectant (column 17, lines 65-66), so it necessarily sterilizes the device. Ryan teaches shipping samples preserved using the device to distant sites, implying use of a packaging means for such transporting (column 3, lines 45-46).

Ryan does not teach an embodiment in which DU and an anticoagulant (EDTA, for example) are contained within a collection device with an internal pressure lower than atmospheric pressure. Ryan does not teach an embodiment in which the active agents are freeze-dried.

Camiener teaches that DU may be evaporated to a solid, dry mass that maintains its fixative ability (Examples 1 and 3 at columns 8 and 9). Camiener suggests a composition comprising DU and EDTA (column 8, lines 13-15). Camiener teaches that lyophilization (freeze-drying) may also be used to dry the fixative (column 9, lines 31-32). The dried fixative of Camiener is suitable for preserving biological materials, including blood (claim 1 and column 7, lines 42-47). Camiener teaches that the solid form may contain between about 0.15% and 62% of an antimicrobial agent, e.g. DU (column 6, line 48, through column 7, line 17, especially column 7, lines 6-7; and column 3, lines 42-62, especially line 55).

Glover teaches a tissue collection device that holds a vacuum inside and may be sealed with a stopper (Abstract). The title of Glover refers to the device as a vacutainer. The device of Glover contains a vacuum sufficient to allow cells to be collected (column 6, lines 36-41). Glover teaches adding a clotting agent after the sample is collected (column 6, lines 53-55).

Louderback teaches that EDTA is an anticoagulant (column 3, lines 30-32).

A person of ordinary skill in the art would have had a reasonable expectation of success in including the dried DU of Camiener within the EDTA-containing evacuated device of Ryan for the purpose of preserving cells because Camiener teaches that drying DU does not affect its preservative properties. The skilled artisan would have had a further expectation of success in employing the evacuated tissue collection device of Glover as the "vacutainer" of Ryan because Glover's device can be used to collect blood. The person of ordinary skill in the art would have had a further reasonable expectation in combining the teachings of Ryan and Glover because Louderback teaches that the EDTA in the container of Ryan prevents clotting, and because Glover's teaching that clotting agents should be added once blood has been collected clearly indicates that clotting prior to processing is undesirable.

The skilled artisan would have been motivated to substitute the dried DU of Camiener for the DU solution taught by Ryan because Camiener teaches that DU maintains its fixative ability after being dried and is useful for fixing and preserving cells, which is the same utility sought by Ryan.

The selection of the amount of DU and EDTA to include in the collection device would have been a routine matter of optimization on the part of the artisan of ordinary skill, said artisan recognizing that Ryan teaches that these amounts may be modified as necessary. A holding of obviousness over the cited claims is therefore clearly required.

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was made to include DU and EDTA within an evacuated container in amounts sufficient to preserve the morphology and antigenic sites of cells stored in said container because Ryan teaches that DU has such preservative activity and because Glover teaches such a partially evacuated device for collecting cells. It would have been further obvious to the skilled artisan in the art at the time the invention was made to dry DU and/or EDTA within the collection device because Camiener teaches that such dried compositions are useful for fixing and preserving collected cells.

Therefore, the invention as a whole would have been *prima facie* obvious to a person of ordinary skill at the time the invention was made.

Claims 5 and 18 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Ryan, Camiener, Glover, and Louderback as applied to claims 1-4, 7, 8, 10, 14-17, 20, 21, 23, and 27-50 above, and further in view of Deich et al. (1992, U.S. Patent 5,110,908).

The teachings of Ryan, Camiener, Glover, and Louderback are relied upon as above. Furthermore, Ryan teaches that samples collected in the device may be used in the preparation of vaccines (column 3, lines 35-39).

Ryan, Camiener, Glover, and Louderback do not teach including a polyacrylic acid in the collection device.

Deich teaches that polyacrylic acid is an adjuvant suitable for use in vaccine production (column 21, line 44, through column 22, line 6).

A person of ordinary skill in the art would have had a reasonable expectation of success in including the polyacrylic acid of Deich in the collection device of Ryan taken in view of Camiener, Glover, and Louderback because Deich teaches that polyacrylic acid may be contacted with vaccines. The skilled artisan would have been motivated to include polyacrylic acid in the collection device to facilitate the production of vaccines, as taught by Ryan.

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was made to include the polyacrylic acid of Deich in the collection device of Ryan taken in view of Camiener, Glover, and Louderback because both are taught as being useful in vaccine production.

Therefore, the invention as a whole would have been *prima facie* obvious to a person of ordinary skill at the time the invention was made.

Response to Arguments

Applicant alleges that the examiner has not considered the claimed ratios. See reply, second page of remarks. Applicant alleges that the art does not teach the claimed ratios. *Id.* Applicant makes numerous allegations about unexpected results and commercial success. *Id.* These arguments have been fully considered, but they are not persuasive.

As an initial matter, the examiner has always considered the claimed ratios to the extent they limit the scope of the claims. The amendments to the claims rectify the defect in previous claim listings by including ratios that clearly limit the relationship of one particular component to another.

However, the fact that the claims appear to include definite ratios does not overcome the examiner's finding of obviousness. Ryan teaches that the amount of fixative relative to the concentration of cells may be varied. For example, claim 19 of Ryan indicates that cells may be preserved by placing them in a solution that contains as little as about 1% DU, i.e. a ratio of about 1:100, which is less than the 2:100 ratio in claim 1. Furthermore, Ryan teaches that any amount that that is "effective to fix or stabilize the tissue or cell membrane" is acceptable. See column 7, lines 39-41. Camiener teaches that as little as 0.15% DU in a dry, solid form in a preservative maintain their properties and can fix tissue. See columns 6 and 7. Applicant has submitted no evidence that the choice of any ratio, claimed or otherwise, yields truly unexpected results.

Applicant also refers to "substantial market success" and unexpected results that "[go] against the conventional wisdom that a small amount of fixative is able to sufficiently disperse within a sample for effective stabilization." This argument is merely the argument of counsel and is unsupported by evidence or declarations of those skilled in the art. Attorney argument is not evidence unless it is an admission, in which case, an examiner may use the admission in making a rejection. See M.P.E.P. § 2129 and § 2144.03 for a discussion of admissions as prior art. Counsel's arguments cannot take

the place of objective evidence. *In re Schulze*, 145 USPQ 716 (CCPA 1965); *In re Cole*, 140 USPQ 230 (CCPA 1964); and especially *In re Langer*, 183 USPQ 288 (CCPA 1974). See M.P.E.P. § 716.01(c) for examples of attorney statements that are not evidence and that must be supported by an appropriate affidavit or declaration.

In preparing a proper affidavit supporting patentability, applicant is encouraged to review M.P.E.P. § 716.01 and its subsections, particularly subsection (b), which provide general guidance for providing evidence to overcome obviousness rejections and define the necessary "nexus." Applicant should also consult § 716.02 regarding unexpected results. § 716.02(b) requires applicant to show by evidence that results are unexpected, unobvious, and of both statistical and practical significance. § 716.03 requires that the applicant bears the burden of establishing a nexus between the claimed invention and the allegations of success. Mere opinion statements (i.e., statements unaccompanied by experimental data or citation to particular art teachings) by an expert or otherwise will be persuasive only to the extent permissible by § 716.01(c), part III.

No claims are allowed. No claims are free of the art.

Applicant is requested to specifically point out the support for any amendments made to the disclosure in response to this Office action, including the claims (MPEP 714.02 and 2163.06). In doing so, applicant is requested to refer to pages and line numbers in the as-filed specification, **not** the published application. Due to the procedure outlined in MPEP § 2163.06 for interpreting claims, it is noted that other art

may be applicable under 35 U.S.C. § 102 or 35 U.S.C. § 103(a) once the aforementioned issue(s) is/are addressed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lora E. Barnhart whose telephone number is 571-272-1928. The examiner can normally be reached on Monday-Thursday, 9:00am - 5:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lora E Barnhart/
Primary Examiner, Art Unit 1651